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10/685,925	10/15/2003	Dwight L. Anderson	110.01840101	7050

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/685,925	**Applicant(s)** ANDERSON ET AL.	
	Examiner Zachariah Lucas	**Art Unit** 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2005*.
2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.
4a) Of the above claim(s) *9-12* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-8 and 13-15* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/18, 3/16 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

1. Currently, claims 1-15 are pending in the application. In the prior action, mailed on December 16, 2004, claims 1-15 were pending, with claims 1-8 and 13-15 under consideration and rejected, and claims 9-12 withdrawn as to non-elected inventions. In the Response of March 16, 2005, the Applicant amended claims 13 and 15.

2. Claims 1-8 and 13-5 are under consideration.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on January 18, and on March 16 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Claim Rejections - 35 USC § 112

4. **(Prior Rejection- Withdrawn)** Claim 15 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim was rejected because it was not clear which binding agent from claim 13 was being referred to in the claim. In view of the amendments to claims 13 and 15, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. **(Prior Rejection- Maintained)** Claims 1-6 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Wilson (U.S. 5,985,596) in view of Olsvik et al. (Clin Microbiol Rev 7:43-54), and Sun et al. (J Indust Microbiol Biotech 25: 273-75). The Applicant presents four general arguments in traversal of this rejection. First, the Applicant argues that there is no suggestion or motivation to combine the indicated references. Second, the Applicant argues that the Examiner has used impermissible hindsight in making the rejection. Third, the Applicant argues that there is no reasonable expectation of success. Finally, the Applicant argues that the combination of the references would not result in the claimed invention. These arguments are not found persuasive.

Motivation to combine and Expectation of Success

The Applicant's first argument in traversal of the rejection is an assertion that there is no motivation for those in the art to combine the indicated references. The third argument is an assertion that there is no reasonable expectation of success in the combination. While the Applicant provides no more than an assertion of a lack of expectation of success, the arguments with reference to the motivation to combine are deemed to apply to both arguments. The Applicant begins by generally describing the teachings of the cited references. As noted by the Applicant, the Wilson reference teaches that the phage used in the process may be removed from the infected sample by "absorbing the exogenous phage particles... on a suitable substrate which can then be separated from the bacterial cells." While the Applicant indicates that such substrates include filter papers, the teachings in patent are more general, and would include any art-recognized means of removing the phage from the sample according to the general description.

Such a means is referred to by Olsvik. While, as suggested by the Applicant, the Olsvik reference is primarily concerned with the use of magnetic separation (MS) of nucleic acids, this does not constitute the entirety of the reference's teachings. Rather, the background of teachings of the reference (e.g. page 43) indicate that it has been shown in the art that MS is useful for the detection of virus particles. These teachings, in conjugation with those of Sun showing the attachment of phage to magnetic particles for removal from a solution demonstrate that this would have been a recognized means of removing phage from a sample by those considering the teachings of Wilson. While Sun is also primarily concerned with the removal of bacterial cells, the reference clearly teachings the attachment of phage particles to the magnetic particles. Although the phage particles are attached to the magnetic beads for the later removal of bacterial cells through MS, the reference also demonstrates that, as suggested by Olsvik, MS would also be useful for the detection and separation of phage particles from a sample. The fact that the references also provide other teachings is noted. However, the teachings of the references as a whole must be considered, and while the references provide other teachings than those relied upon, the other teachings in way teach away from the use of MS for the separation of phages as used in the present methods.

The Applicant argues that none of the references provides a motivation to combine the their teachings one with another. However, the motivation to combine the references need not be explicit in the art. See e.g., MPEP § 2144. One such non-explicit source of motivation is the substitution by those in the art of equivalents known for the same purpose. MPEP § 2144.06. In the present case, the Wilson reference provides general teachings regarding a method involving the removal or inactivation of phage from a sample. While the reference provides some examples of means falling within the scope of such inventions, the teachings of the reference also indicate that any means known in the art would suffice. The combination of Sun and Olsvik demonstrate that MS, using biotin/streptavidin binding to attach the phage to a magnetic bead, would have been both recognized by those in the art, and would have been expected to work. This is because the teachings of Olsvik suggest that MS would be so useful, and the teachings of Sun illustrate a method of separating bacteria from a sample which could only work if the method would also be capable of effectively removing phage. Thus, the teachings in the art both provide adequate motivation to combine, and provide a reasonable expectation of success in the combination. The Applicant's first and third arguments are therefore not found persuasive.

Impermissible Hindsight

In response to applicant's argument (the second argument in traversal) that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, as was illustrated above and in the prior action, the Examiner has applied only teachings that were known in the art at the time the claimed invention was made. The Applicant has not pointed out any feature of the claimed invention for which support could only have been taken from the teachings of the present application. The third argument in traversal is therefore not found persuasive.

The Claimed Invention

The Applicant's fourth and final argument presented with respect to this rejection is an assertion that the combination of the cited references would not result in the claimed invention. In support of the assertion, the Applicant goes step by step through the claim asserting that each of these steps is not addressed by the references. The arguments are not found persuasive.

With respect to the bacteriophage comprising the binding agent, and the substrate comprising an immobilized ligand for the binding agent, the Applicant is directed to the teachings of Sun and Olsvik as described above, and in the prior action. In particular, the teachings of Sun illustrate that those in the art were aware of the use of biotinylated phage such that they could be captured onto streptavidin labeled magnetic beads, thereby meeting the limitations described in the first three paragraphs of the Applicant's argument on page 11 of the Response. The fourth paragraph of page 11 refers to the removal of the bacteriophage/binding agent complex. This would read on the removal of the phage complexed to the magnetic beads as is also suggested by Sun and Olsvik. Thus, the combined references also account for this limitation.

On page 12, the Applicant also asserts that the teachings of the references do not account for the detection of the new bacteriophage. However, as the primary reference, Wilson, teaches that the formation of new phage are detected through a plaque analysis, this limitation is also met by the cited combination of references.

As is described above, and in the prior action, the cited references teach or suggest each of the limitations of the rejected claims. For the reasons above and of record, the Applicant's arguments in traversal of this rejection are not found persuasive. The rejection is therefore maintained.

7. **(Prior Rejection- Maintained)** Claims 7 and 8 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Wilson, Olsvik, and Sun as applied above, and further in view of Teodorescu et al. (U.S. 4,797,363). The Applicant traverses the rejection on the grounds provided with respect to claims 1-6 above, and through an assertion that Teodorescu does not teach the additional limitations of claims 7 and 8 (the detection of the new bacteriophage through the use of a fluorescent dye or nanocrystal). The arguments not specific to claims 7 and 8 have been addressed above.

With respect to claims 7 and 8, the Applicant argues that Teodorescu does not teach the additional limitations of these claims. In prior action, the Examiner pointed out where in its teachings Teodorescu disclosed the indicated limitations. See, col 3, esp. lines 60-64, and col 9, lines 43-65 of the reference. The reference is concerned with the detection of phage in a sample, and indicates that the disclosed methods using fluorescent dyes avoids the necessity of taking time to grow and culture the bacterial sample. Column 3. Thus, the reference both teaches the indicated means of detecting phage in a sample, and provides a motivation to use such methods over the plaque assay used by Wilson. The Applicant's assertion that the reference does not provide these teachings is therefore not found persuasive. The rejection is therefore maintained for the reasons above, and the reasons of record.

8. **(Prior Rejection- Maintained)** Claims 13-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Wilson, Olsvik, and Sun as applied above, and further in view of Yazdankhah et al. (Vet Microbiol 62:17-26). The Applicant traverses this rejection this rejection on 1) the grounds asserted with respect to claim 1-6 above, 2) by asserting that there is no motivation to combine the teachings of Yazdankhah with those of the other cited references, and 3) that the teachings of the cited references do not teach each limitation of the claimed inventions. With respect to the first argument in traversal, the same as asserted with respect to claims 1-6 above, the argument is not found persuasive for the same reasons as discussed with respect to claims 1-6 above.

The second argument presented is an assertion that there is no motivation to combine the teachings of Yazdankhah with those of the previously cited references. The Applicant provides two arguments in support of the assertion. First, the Applicant argues that there is no motivation to combine the teachings of Yazdankhah, which relate to the detection of bacterial cells using magnetic beads, with the teachings of Wilson, which relate to methods of using phage to detect bacteria, or with Olsvik, which generally teaches methods of assaying nucleic acids using magnetic beads. The Applicant appears to be arguing that, due to the different focus of each of these references, those in the would have had no motivation to combine their teachings. This argument is not found persuasive. The teachings of Wilson and Olsvik have been described above. While the primary teachings of Olsvik are related to the claimed invention, the reference nonetheless provides teachings directing those in the art to the use of magnetic separation (MS) for the detection of phage particles. Further, the reference indicates that the MS is useful for the detection "of prokaryotic organisms such as bacteria and viruses," indicating that MS is a generic method, the teachings of which can be broadly applied to the detection of various organisms and analytes.

Yazdankhah is also concerned with the use of MS for the detection of bacterial cells. However, a review of the reference, in combination with those of Sun and Olsvik, shows that the methods disclosed therein are similar to those of the other references, albeit targeting a different microorganism. However, because the methods used in these references are so similar, and because the use of antibodies to detect phages is known in the art, it would have been obvious to those in the art that the MS method of Yazdankhah could also be used for the detection of phage. Because such MS methods are disclosed in the art as more rapid than those requiring the culturing of bacteria, such as in the plaque assay used by Wilson, those in the art would have been motivated to use MS for both the removal of the parent phage, and for the detection of the progeny phage. Further, because the progeny phage would not comprise the biotin label required for the biotin/streptavidin mode of capture, it would have been obvious to those in the art to use other means of immobilizing the progeny phage, including through the use of antibodies. Thus, the art both provides adequate motivation and suggestion to combine the references. The Applicant's second argument in traversal of this rejection is therefore not found persuasive.

The third argument in traversal of this rejection is substantially the same as the fourth argument in traversal of the rejection of claims 1-6. The only additions to the argument is the further assertion that Yazdankhah does not cure the previously asserted defects in the rejection, and that Yazdankhah does not teach the detection of the progeny phage according to the claimed invention. These arguments are not found persuasive. The assertions with respect to the limitations with respect to the first phage were addressed above with respect to claims 1-6. The assertions with respect to the complexing and detection of the new phage are not found persuasive in view of the discussion of the rejection of claims 13-15 presented in the prior action, and above with respect to the motivation to combine references.

Because the Applicant's arguments in traversal are not found persuasive for the reasons above, and the reasons of record, the rejection is maintained.

Conclusion

9. No claims are allowed.

10. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> WO 93/17129. This reference is considered redundant to the teachings of Sun, in that the reference teaches the conjugation of a phage with biotin such that it may be captured by an avidin-coated substrate. See e.g., pages 9-10.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel
5/16/05

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